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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/448,378	11/23/1999	KENNETH BRASEL	2836-D	4973

22932 7590 11/17/2005

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/448,378	BRASEL ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,20,22-26,28,30-35,37 and 39-56* is/are pending in the application.

4a) Of the above claim(s) *54-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,20,22-26,28, 30-35, 37, 39-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 10/12/05, has been entered.

Applicant's amendment, filed 10/12/05, has been entered.

Claims 6 and 20 have been amended.

Claims 1-5, 8-19, 21, 27, 29, 36 and 38 have been canceled previously.

Claims 6, 7, 20, 22-26, 28, 30-35, 37, 39-56 are pending.

Applicant's election without traverse of Group I and the species GM-CSF has been ackno

Claims 54-56 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's amendment, filed 10/12/05.

The rejections of record can be found in the previous Office Actions.

3. As indicated previously, the filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/539,142, i.e. 10/4/95.

4. Upon reconsideration of applicant's amended claims, filed 1/12/05, the previous rejection under 35 U.S.C. § 112, first paragraph, written description, has been withdrawn.

5. Claims stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lyman et al. (WO 94/94/28391; 1449) in view of Elliott et al. (U.S. Patent No. 5,478,556), Srivastava et al. (U.S. Patent No. 6,017,544) and Brem et al. (U.S. Patent No. 5,626,862) essentially for the reasons set forth in the previous Office Actions.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Here, applicant does focus their argument that the prior art separately or together do not teach or suggest that administration of flt3-ligand will generate flt3-ligand-derived dendritic cells that can augment immune responses to tumor antigens.

Applicant is reminded that the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon , 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied , 500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300,

1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done " (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.

Therefore, the reason or motivation to combine may often suggest doing what the inventor has done, but for a different purpose or to solve a different problem than that asserted by the inventor. See MPEP 2144.

The strongest rationale for combining references is a recognition in the art that some advantage or expected beneficial result would have been produced by their combination. This recognition may be an expressed statement in a reference, an implication that can be drawn from one or more references or a convincing line or reasoning based upon established principles or legal precedent.

Therefore the rejection of record is maintained for the reasons of record and addressed above and reiterated for applicant's convenience.

The instant claims are drawn to methods of augmenting immune responses in cancer patients with FLT3-ligand and GM-CSF.

Lyman et al. teach methods of treating cancer patients by administering FLT3-L in combination with other cytokines, including GM-CSF including treating intestinal damage resulting from irradiation and chemotherapy and stimulating immune responses as well as hemopoietic cells to improve the quality of life of a patient (see entire document; Background of the Invention; Summary of the Invention, including Claims). Lyman et al. teach the FLT3-L and its recombinant forms and sequences encompassed by the claimed invention (See Detailed Description of the Invention and Examples).

Lyman et al. differs from the claimed methods by not disclosing the known administration of a tumor antigen to a cancer patient to induce an immune response to the desired tumor antigen and that the administration of FLT3-L and/or GM-CSF would lead to an increase in the number of dendritic cells per se.

Both Elliott et al. and Srivastava teach that GM-CSF teach the known administration of GM-CSF with tumor antigens to simulate the immune system.

Elliott et al. teach the vaccination of cancer patients with tumor associated antigens mixed with cytokines, including GM-CSF, including the stimulation of antigen-processing (see entire document, Background of the Invention, Summary of the Invention, Detailed Description of the Invention). Both the tumor associated antigens and the GM-CSF can be administered at various times (see Summary of the Invention).

Srivastava teach methods of augmenting cancer vaccines with cytokines including GM-CSF (see entire document; including Summary of the Invention, including column 4, paragraph 6; Detailed Description, including column 12, paragraph 3; Claims.). Srivastava teach compositions comprising cancer cells as well as cancer antigens serve as sources for immunization against tumor antigens of interest (See entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention). In addition to combining cancer therapies, including surgery, radiation therapy and chemotherapy (columns 5-6, overlapping paragraph), dosages and modes of administration depend on variables known and practiced in the art at the time the invention was made (e.g. see columns 11-12, Formulation and Administration of the Complexes). Srivastava teach that a number of tumor types, including fibrosarcoma, can treated (see column 6, paragraphs 4-5).

Brem et al. teach the GM-CSF is a cytokine that systematically activate cytotoxic T lymphocytes which have shown to lead to the elimination of tumor cells in a potent and specific manner, by stimulating the growth and activity of several myeloid cells and playing a critical role in the migration and development of professional antigen presenting cells such as dendritic cells (see column 8, paragraph 2).

Given the teachings of combining FLT3-L and GM-CSF to treat cancer by Lyman et al. in combination with the teachings of Elliott et al. and Srivastava et al. that GM-CSF was potent in cancer vaccination, one of ordinary skill in the art would have combined FLT3-L, GM-CSF and tumor antigens to stimulate the hemopoietic and immune system of cancer patients, including the vaccination to tumor associated antigens. Given the teachings of stimulating the hemopoietic and immune systems with FLT3-L and GM-CSF with the teachings of administering tumor antigens to activate immune responses and antigen presentation, one of ordinary skill in the art would have had an expectation of success that the administration of FLT3-L and GM-CSF would increase the number of dendritic, as evidenced by the teachings of Brem et al. that GM-CSF activates immune responses via dendritic cells.

Given the teachings of the prior art to treat and augment immune responses in cancer patients and that the administration of cytokines and tumor antigens were based on variables and procedures known and practiced by the ordinary artisan, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer tumor antigen at various times with respect to cytokine administration, including the administration of tumor antigen prior, concurrently and after cytokine administration.

One of ordinary skill in the art at the time the invention was made would have been motivated to select a combination of cytokines, including FLT3-L and GM-CSF in combination with tumor antigens to treat human cancer; given the properties of said cytokines to augment immune responses including augmenting immune responses to cancer antigens and to stimulate hemopoietic cells to alleviate the effects of chemotherapy and radiation therapy in cancer patients.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

Again, the reason or motivation to combine may often suggest doing what the inventor has done, but for a different purpose or to solve a different problem than that asserted by the inventor. See MPEP 2144.

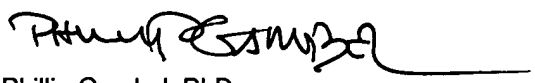
Here, the prior art provides sufficient motivation and expectation of success in arriving at the same maniupulative steps as the claimed invention in treating patients having cancerous or neoplastic disease.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, PhD.
Primary Examiner
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November 14, 2005